1: Transplantation. 2000 Apr 15;69(7):1304-10. Related Articles, L

Comment in:
- Transplantation. 2000 Apr 15;69(7):1233-4.

Induction of xenoreactive CD4+ T-cell anergy by suppressor CD8+CD28- T cells.

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BACKGROUND: The underlying mechanism of immune suppression media by regulatory T cells is not completely understood. In previous studies we ha shown that antigen-specific human T suppressor cells (Ts) can be generated i vitro by multiple rounds of stimulation with allogeneic, xenogeneic, or antige pulsed autologous antigen-presenting cells (APC). Human Ts express the CD8+CD28- phenotype and require specific recognition of MHC class I/pept complexes on the surface of APC to block proliferation of T helper cells (Th) The aim of the present study was to explore the activation requirements of Ts well as the nature of Th unresponsiveness to xenogeneic (swine) antigens induced by Ts. METHODS AND RESULTS: We investigated whether speci antigenic stimulation of Ts is required for their ability to inhibit early activati of xenoreactive Th (up-regulation of CD40 ligand). Flow cytometry studies indicated that Ts function required specific recognition of MHC class I on th surface of the stimulating APC. However, neither proliferation nor protein synthesis was required for the ability of Ts to inhibit Th. Ts drastically reduc the capacity of xenoreactive Th cells to produce interleukin (IL)-2 in respons the specific APC, without affecting their surface expression of IL-2 receptor. The suppressor effect that Ts exerted on Th proliferation could not be circumvented by CD40 ligation on the surface of the APC but could be rever by the addition of exogenous IL-2. CONCLUSION: These data indicate that induce anergy of xenoreactive human Th cells upon specific recognition of MHC class I antigens. Hence, Ts may prevent the activation of T cell-mediat immune responses against xenogeneic transplants.

PMID: 10798745 [PubMed - indexed for MEDLINE]